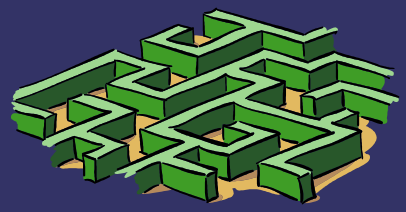
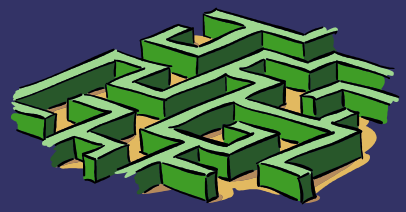
Introduction to Computer Methods in Molecular Structure

The objective of this set of lectures and laboratories is to provide students with a basic knowledge about some of the computational resources related to studies in the field of computational biology, and to enable them to use some of these tools.



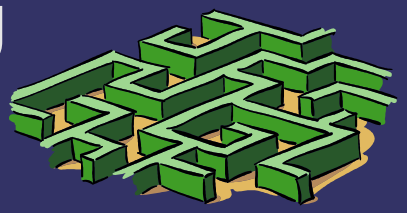
Overview

- Molecular Graphics Software
  - for publication, visual presentation, and analysis
- Structure and Dynamics Prediction
  - needed for understanding function in
    - protein chemistry
    - protein – DNA interactions
    - protein – ligand binding
      - intelligent structure based drug design



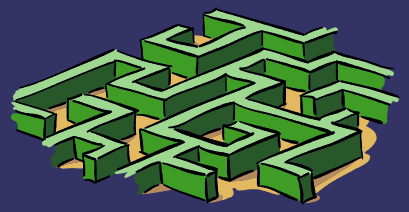
Molecular Graphics Software

- Rasmol/Raswin
  - for viewing protein structures and producing publication figures
- Protein Explorer
  - uses Rasmol in a user-friendly wrapper
- VMD (Visual Molecular Dynamics)
  - for viewing and analysing molecular dynamics simulations and building dynamics movies



Structure and Dynamics Prediction

- Protein structure and prediction
  - X-ray and neutron diffraction, and NMR, provide experimentally known 3D structures.
  - *Ab initio*: Go to 3D structure from sequence only.
  - Comparative modeling (comparisons to knowns).
- Prediction of dynamic (function) properties
  - Can use known 3D structures
  - Quantum Mechanics (QM)
  - Molecular Mechanics (MM)



Quantum Mechanics

- required for covalent bond breaking-making
- first principles approximate solutions to the Schrödinger wave equation, *ab initio*
- not practical for large proteins, expensive
- used to calculate parameters for Molecular Mechanics potential functions (see below)
- used in combined QM/MM methods for large proteins (Gaussian ONIOM)

Molecular Mechanics

- not useful for making and breaking bonds
- calculates molecular energy using classical potential functions with theoretical (from QM) and empirical parameters
- There are many MM force fields available.
- used to refine predictions of 3D structure in
  - Modeler
  - SWISS-MODEL (accessed by Deep View)